

CLINICAL AND EPIDEMIOLOGY RESEARCH ON OSTEOPOROSIS

NIH GUIDE - Vol. 20, No. 7, February 15, 1991

RFA NUMBER: AR-91-03

P.T. 34; K.W. 0705050, 0785055, 0760020, 0760025, 0755030, 0745027

National Institute of Arthritis and Musculoskeletal and Skin Diseases

National Institute of Diabetes and Digestive and Kidney Diseases

Letter of Intent Receipt Date: April 1, 1991

Application Receipt Date: May 15, 1991

INTRODUCTION

Osteoporosis is a disease characterized by low bone mass, microarchitectural deterioration of bone tissue, and a consequent increase in fracture risk. Osteoporosis represents a major public health problem in the United States, exacting an enormous societal toll annually in morbidity and mortality. It affects more than 24 million Americans and is responsible for at least 1.3 million fractures each year. Moreover the frequency of osteoporosis and osteoporosis-related fractures is expected to increase with the expansion of the elderly population in the upcoming decades.

Bone mass in the adult skeleton reflects the accumulation and maintenance of bone tissue during growth and maturation, and the rate and duration of bone loss thereafter. Factors that induce a low peak bone mass and those that underlie excessive postmenopausal and aging associated bone loss predispose an individual to osteoporosis. Although our knowledge is incomplete, genetic, endocrine and lifestyle factors are contributory. The development and testing of strategies for building and maintaining an adequate bone mass and preventing bone loss are essential.

BACKGROUND

A national scientific conference on RESEARCH ADVANCES IN OSTEOPOROSIS, sponsored by National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and the National Institute on Aging, was held in February 1990.

Following the general meeting, the NIAMS convened a meeting of leaders in basic and clinical osteoporosis research to develop future research directions and opportunities. These research directions became part of a report that was requested last year by the Senate Appropriations Committee. The Report on HHS-wide Research, Education, and Health Promotion Activities in Osteoporosis also contained information on the status of current research in osteoporosis throughout the Department of Health and Human Services. A copy of this report may be requested by contacting Dr. Joan McGowan at the address listed below. As follow-up to the report to the Senate Appropriations Committee and to be responsive to current congressional interest and support for osteoporosis research, a Request for Applications (RFA) is proposed to solicit applications in the particular areas of clinical and epidemiologic research that are specifically and directly applicable to osteoporosis.

RESEARCH GOALS

This RFA is intended to foster and enhance research specifically directed to prevention and treatment strategies, as well as epidemiologic studies of osteoporosis. Some of these areas, identified as needing additional research, are listed below:

- o Studies on maximizing bone mass in early life
- o Biochemical markers of bone remodeling
- o Non-invasive measurement of bone density/mass and structure
- o Further studies of sex hormone use in osteoporosis
- o Role of exercise in prevention and treatment of osteoporosis
- o Development of hormone analogs with specific therapeutic application in osteoporosis
- o Therapeutic potential for growth factors
- o Incidence and etiology of osteoporosis in men and blacks
- o Etiology of juvenile and adult idiopathic osteoporosis
- o Additional research on risk factors

- o Research on prevention strategies

Other clinical and epidemiologic research applications in the field of osteoporosis are encouraged. In order to be considered responsive to this RFA, applications must be specifically directed to osteoporosis.

MECHANISM OF SUPPORT

This RFA will use the traditional National Institutes of Health (NIH) research project grant (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000, revised October 1, 1990.

Approximately \$2,000,000 in total costs per year for three to five years will be committed by the NIAMS specifically to fund applications that are submitted in response to this RFA. The NIDDK will provide additional funds to support approximately two projects. The funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. The total project period for applications submitted in response to the present RFA may not exceed five (5) years. The earliest possible start date for the initial awards will be September 30, 1991. Although this program is provided for in the financial plans of the NIAMS and the NIDDK, award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose. Applications may receive secondary assignment, when appropriate, to the National Institute on Aging, which may fund projects in addition to those funded by NIAMS and NIDDK. Non-profit and for-profit institutions, and foreign as well as domestic institutions, are eligible to apply.

This RFA is a one-time solicitation. Generally, future unsolicited competing renewal applications that result from this RFA will compete as research project applications with all other investigator-initiated applications and be reviewed in a standing Division of Research Grants study section. However, should it be determined that there is a sufficient continuing program need, NIAMS and NIDDK may announce a request for renewal applications.

REVIEW PROCEDURES AND CRITERIA

REVIEW PROCEDURE

Upon receipt, applications will be reviewed initially by the Division of Research Grants for completeness. Incomplete applications will be returned to the applicant without further consideration. Evaluation for responsiveness to the RFA is an NIAMS and NIDDK program staff function. Applications that are judged non-responsive will be returned to the applicant but may be submitted as investigator-initiated applications at the next receipt date. Questions concerning the relevance of proposed research to the RFA should be directed to program staff as described in INQUIRIES.

In cases where the expected number of applications is large compared to the number of awards to be made, the NIH will conduct an administrative prereview (triage) to eliminate those that are clearly not competitive. The NIH will withdraw from further competition those applications judged to be noncompetitive and notify the applicant and institutional business official.

Those applications judged to be both responsive and competitive will be evaluated in accordance with the criteria stated below for scientific/technical merit by an appropriate initial review group convened by the NIAMS Review Branch. The second level of review by the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council, the National Institute of Diabetes and Digestive and Kidney Diseases National Advisory Council and, in some cases, the National Advisory Council on Aging will make recommendations regarding funding.

REVIEW CRITERIA

Proposals responsive to this competitive solicitation will be reviewed in accordance with the following criteria:

1. Extent of relevance of the proposed research to the aims of the RFA.
2. Scientific merit of the proposed approach, including the adequacy and quality of the methodological approach and the research design. Familiarity with the proposed techniques should be demonstrated, e.g., by the presentation of preliminary data.
3. Expertise and qualifications of the Principal Investigator and proposed staff and/or collaborators to perform the proposed experiments.
4. Documentation of the adequacy of the facilities and resources.

The review group will examine critically the proposed budget and recommend an appropriate budget for each approved application.

SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAHMA policy is that applicants for NIH/ADAHMA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study group must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Section 2, A-D of the Research Plan and summarized in Section 2, E, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, the NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans, Asian/Pacific Islanders, Blacks, Hispanics)

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of the research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained in the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to the scientific question(s) addressed and the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

METHOD OF APPLYING

The grant application form PHS 398 (revised 10/88) must be used in applying for these grants. These forms are available at most institutional business offices and from the Office of Grants Inquiries,

Division of Research Grants, National Institutes of Health, Westwood Building, Rm. 449, 5333 Westbard Avenue, Bethesda, Maryland 20892.

The RFA label available in the 10/88 revision of form PHS 398 must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the title of the RFA and the RFA number must be typed on line 2 of the face page of the application form.

Submit a signed, typewritten original of the application, including the Checklist, and four (4) signed, exact photocopies, in one package to the Division of Research Grants at the address below. The photocopies must be clear and single sided.

DIVISION OF RESEARCH GRANTS

National Institutes of Health
Westwood Building, Room 240

Bethesda, MD 20892**

At the time of submission, two (2) additional copies of the application must also be sent to:

REFERRAL OFFICER

Division of Extramural Activities

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Westwood Building, Room 5A-07

5333 Westbard Avenue

Bethesda, MD 20892

Applications must be received by May 15, 1991. If an application is received after that date, it will be returned to the applicant. If the application submitted in response to this RFA is substantially similar to a research grant application already submitted to the NIH for review, but has not yet been reviewed, the applicant will be asked to withdraw either the pending application or the new one. Simultaneous submission of identical applications will not be allowed, nor will essentially identical applications be reviewed by different review committees. Therefore, an application cannot be submitted in response to this RFA that is essentially identical to one that has already been reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

INQUIRIES

Written or telephone inquiries concerning the objectives and scope of this RFA or inquiries about whether or not specific proposed research would be responsive are encouraged and should be directed to:

Dr. Joan A. McGowan

Bone Biology and Bone Diseases Program Director

National Institute of Arthritis and Musculoskeletal and Skin Diseases

5333 Westbard Avenue

Westwood Building, Room 403

Bethesda, MD 20892

Telephone: (301) 496-7495

or

Dr. Ronald Margolis
Director, Endocrinology Research Program
Division of Diabetes, Endocrinology and Metabolic Diseases
NIDDK/NIH
5333 Westbard Avenue
Westwood Building, Room 605
Bethesda, MD 20892
Telephone: (301) 496-7504

The program directors welcome the opportunity to clarify any issues and answer questions from potential applicants.

LETTER OF INTENT

Prospective applicants are asked to submit, by April 1, 1991, a letter of intent that includes a descriptive title of the proposed research, the name and address of the Principal Investigator, the names of other key personnel, the participating institutions, and the number and title of the RFA in response to which the application is being submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains is extremely helpful in planning for the review of applications. It allows NIAMS staff to estimate the potential review workload and to avoid possible conflict of interest in the review.

The letter of intent should be sent to Dr Joan McGowan at the address listed above.

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research and No. 93.855 Diabetes, Endocrinology and Metabolism Research. Awards will be made under authorization of the Public Health Service Act, Title III, Section 301 (c) (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.